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09/674,819	11/06/2000	Akira Aomatsu	5774-01-MJA	5038

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EXAMINER

WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

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05/29/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Status of Claims

Claims 28, 35-37, 40-41 and 43 are pending and under examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicants amendment to the specification which claim priority to the other prior applications e.g., PCT is acknowledged.

Withdrawn Rejection

In view of applicants' arguments the 35 USC 112, second paragraph has been partly overcome.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention for reason set forth below for the maintained rejection.

2. Claim 43 appears to be drawn more to a process claim rather than a composition claim. Non-sequitur for "the content of the corresponding lactam" and "the initial amount".

Response to Arguments

Applicants submit that claim 43 is a composition claim that contains functional elements relating to the stability of the solid composition which is explicitly permitted by MPEP §21735.05(g). Additionally, one skilled in the art readily understands the scope of the claim and can ascertain whether a composition is covered by claim 43.

In reply, the first part of the rejection has been overcome by applicants' arguments. However, the lack of antecedent basis (non-sequitur) for "the content of the corresponding lactam" and "the initial amount" rejection has not been overcome by the above argument.

Claim 40, as amended, is inconsistent with the disclosure of the composition being in a pharmaceutical preparation in the form of tablets, granules or capsules. Thus, it is unclear as to how the stabilized composition becomes tablets or granules or

capsules without formulating into tablets, granules or capsules form.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 28, 36, 40-41 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Lan (20020037926) for reasons of record as repeated below. (See the Schrier rejection below with respect to applicants' priority claim).

Lan discloses at paragraph:

[0028] Gabapentin and pregabalin can be formulated to provide greater stability to the compound. Useful excipients for inclusion with gabapentin and pregabalin include neutral amino acids, such as glycine and L-valine; and humectants, such as ethylene glycol, propylene glycol and glycerine. The active compounds may also be coated as agglomerated powders with a polymer such as polyvinyl pyrrolidone to provide better stability and processing characteristics.

Response to Arguments

Applicants argue that the priority date for the present claims predates the prior art date of paragraph [0028] cited above in Lan (20020037926). The present claims are supported by at least the May 10, 1999, PCT filing on which the U.S. filing is based. In contrast paragraph [0028] of Lan cited

in the Office Action appears to only be entitled to Lan's April 10, 2000, PCT filing date, which is after the priority date of the claimed invention. Provisional application 60/128,543 on which Lan (20020037926) is based does not include the paragraph cited in the Office Action and does not appear to use the term "humectant" or disclose propylene glycol. Accordingly, applicants respectfully submit that Lan (20020037926) is not prior art to the present claims and respectfully request the Examiner withdraw this rejection.

In reply, attention is drawn to e.g., page 22, lines 8-32 of Lan's provisional application S.N. 60/128,543 which positively recites said propylene glycol.

Claim Rejections - 35 USC § 103

Claims 28, 36, 40 and 41 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative under 35 U.S.C. 103(a) as obvious over Schrier et al. (WO 98/58,641).

For claim 28, Schrier et al disclose a composition of pregabalin (pg. 3, lines 19-22). The composition comprise the active compound, pregabalin in dosage unit forms with a pharmaceutical carrier (see e.g. pg. 4, line 17 thru pg. 5, line 11). The pharmaceutical carrier includes pharmaceutical propylene glycol and sorbitol (see e.g. pg. 4, lines 22-28).

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For claim 36, Schrier et al. disclose that the composition also include other component such as coloring agents, flavoring agents, and/or preservatives (refers to instant claimed an auxiliary agent)(see e.g. pg. 4, line 31 thru pg. 5, line 2).

For claim 40, Schrier et al. disclose that the dosage unit forms include tablets, capsules and pills (see e.g. pg. 4, lines 19-22).

For claim 41, Schrier et al. disclose that the compositions are produced by formulating the active compound in dosage unit form with a pharmaceutical carrier that includes diluent (see e.g. pg. 4, lines 17-31).

The claimed property of the composition i.e., a stabilized composition is inherent to the composition of Schrier since Scheier discloses the same composition as claimed.

Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972); *In re Best* 195 USPQ 430 (CCPA 1977).

Applicant is not entitled to the priority date of the Japanese foreign patent in the absence of an English translation. The provisional application also relied for its earlier filing date does not disclose the pregabalin derivative. It appears that said Japanese foreign application corresponds to the provisional application and thus does not also disclose pregabalin. (Note the provisional and Japanese application contain only 24 pages compare to the instant specification of 75 pages). Said pregabalin is disclosed only in the PCT application

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filed on 5/10/99. Thus, the Schrier reference (Dec. 30, 1998) predates the instant PCT application filing date with respect to pregabalin and therefore is a proper reference.

Response to Arguments

Applicants stated that the compositions disclosed in WO 98/58,641 may be solid or liquid and the carriers may be any number of things. Additionally, WO 98/58,641 does not specifically set out the claimed solid dosage form of pregabalin or gabapentin and propylene glycol. Applicants also note that in the list of carriers cited from WO 98/58,641 propylene glycol is listed between vegetable oils and water, which suggests to those skilled in the art that propylene glycol is provided as a carrier for a liquid dosage form. Accordingly, WO 98/58,641 does not specifically disclose the claimed compositions and does not suggest that the inclusion of propylene glycol into solid compositions of gabapentin or pregabalin would provide any stabilizing effect.

In reply, as acknowledged by applicants Schrier teaches also a solid and alternatively disclosed a liquid composition. Schrier at e.g., page 4, lines 22-28 mentioned propylene glycol after the vegetable oil (please note the semicolon separating the lists of vegetable oil from

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propylene glycol). The dosage form is disclosed by Schrier at e.g., page 5, lines 6-15:

The percentage of the active ingredients in the foregoing compositions can be varied within wide limits, but for practical purposes it is preferably present in a concentration of at least 10% in a solid composition.... The most satisfactory compositions are those in which a much higher proportion of the active ingredient is present, for example, up to about 95%. Routes of administration of the GABA analog or its salts are oral.... For example... a useful oral dosage is between 20 and 800 mg. The dosage is within the dosing range used in treatment of inflammatory diseases such as arthritis, or as would be determined by the needs of the patient as described by the physician.

As stated above the stabilizing effect of the composition is a property that would be inherent to Schrier's composition since the components are the same. One having ordinary skill in the art would know that the composition is stable. Such property is necessary in order to formulate into a pharmaceutical composition to be effective in treatment of e.g., disease.

Claims 28, 36, 40 and 41 are rejected under 35 U.S.C. 102(f or g) as anticipated by or, in the alternative under 35 U.S.C. 103(a) as obvious over Schrier et al (USP 6,329,429) for the same reasons as repeated below.

Applicant appears not to have invented the instant claimed composition as evident from the Schrier et al patent.

See the above rejection.

Response to Arguments

Applicants note that U.S. patent no. 6,329,429 is a national stage application of WO 98/58,641 discussed above and that the disclosures of these references appear to be identical. Accordingly, applicants respectfully submit that the rejected claims are not anticipated or rendered obvious by U.S. patent no. 6,329,429 for the reasons discussed above.

In reply, for also the reasons discussed above the claimed invention is anticipated or obvious over the teachings of Schrier ('429 Patent).

Claims 28, 36, 40 and 41 are rejected under 35 U.S.C. 102(f or g) as anticipated by or, in the alternative under 35 U.S.C. 103(a) as obvious over Schrier et al (USP 6,329,429).

Applicant appears not to have invented the instant claimed composition as evident from the Schrier et al patent for reasons as reiterated below.

See above rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300).

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Commonly assigned US Patent 6,329,429, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Double Patenting

Claims 28, 36, 40 and 41 are rejected on the ground of nonstatutory double patenting over claims 1 and 8 of U. S.

Patent No. 6, 329,429 since the claims, **if allowed, would improperly extend the "right to exclude" already granted in the patent** for reasons of record as repeated below.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the instant claimed composition is disclosed by Schrier, (see equivalent WO 98/58,641) above, as used in the claimed method by Schrier.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Response to Arguments

Applicants state that according to the MPEP: Since the doctrine of double patenting seeks to avoid unjustly extending patent rights at the expense of the public, the focus of any double patenting analysis necessarily is on the claims in the multiple patents or patent applications involved in the analysis... MPEP §804 (emphasis added). Additionally A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). MPEP §804 II.B.1. (emphasis added). The claims in the present application are directed to a stabilized solid composition comprising pregabalin or gabapentin and propylene glycol. In contrast, claims 1 and 8 of U.S. patent no. 6, 329,429 are for "method[s] for preventing and treating inflammatory disease[.]"

In reply, a double patenting rejection is also appropriate when the subject matter claimed in the instant application is **fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter**. See above. The claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

Thus, the disclosure of the patent which disclosed the instant composition renders the claimed obvious.

Claims 28, 35-37, 40-41 and 43 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wallace (US 5,025,035) or 5,084,479 (Woodruff) for reasons set forth in the last Office action and reiterated below.

Wallace and Woodruff disclose compositions of gabapentin and other 4-amino-3-substituted-butanoic acid derivatives with propylene glycol; see col. 2, lines 13-57 of Wallace and Example 3. See Woodruff at col. 3, line 35 to col. 4, line 12.

See the above rejection under Schrier (WO 98/58641).

Response to Arguments

Applicants traverse these rejections for the same reason as WO 98/58,641 discussed above. In fact, the sections of the patents cited in the Office Action appear to be virtually identical to that in WO 98/58,641. Example 3 of U.S. patent no. 5,025,035 cited in the Office Action also makes no mention of propylene glycol.

In reply, for the same reasons discussed above under WO 98/58,641 is incorporated herein in response to applicants' arguments.

Claim Rejections - 35 USC § 103

Claims 28, 35-37, 40-41 and 43 are rejected under 35 U.S.C. 103(a) as being obvious over Augart et al (US 6,054,482) in view of any one of Giacini (US5302373), Herget (US5618342) or Baschang (4666886).

Augart et al (US'482, hereafter) teach a stable solid composition in the form of tablet or capsules (dry medicinal forms) and a process for the preparation thereof, wherein the composition comprises a cyclic amino derivative of the general formula I such as gabapentin as an active agent and an adjuvant materials (e.g. polyethylene glycol), see abstract, col. 2,

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lines 27-30, claims (especially, claim 4, (c) and claim 8) and column 3 lines 25-45. It is noted that the specific adjuvants of US'482(i.e., polyethylene glycol) are conventionally known as humectants and naturally play the role as "humectant" that is any substance added to another substance to keep the moisture. Any compound of the said adjuvants of US'482 would be used to prevent the excess water available for forming undesirable lactam. Thus, the cited reference discloses that said compounds (e.g., polyethylene glycol) carry out the stabilization of the active agent from lactam formation whether they are called humectant or not. For instance, the stabilizing activity carried out by the said compounds is enabled in US'482 wherein the formation of lactam (byproduct) that is usually associated with certain toxicities can be suppressed by the preferred adjuvants (e.g., polyethylene glycol, see column 4, lines 60 thru column 5, lines 33). Augurt does not disclose one of the glycols i.e., propylene glycol as claimed. However, Herget or anyone of the above secondary references discloses the functional equivalence of propylene and ethylene glycol as humectant.

US'373 teaches that propylene glycol, glycerol, sorbitol, or cyclodextrin is functionally equivalent humectant, see column 2, lines 28-33.

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US'342 teaches that glycerol, substituted glycerol, sorbitol, polyethylene glycol, polypropylene glycol, polyvinylpyrrolidone is functional equivalent humectant, see claim 3.

Baschang discloses at e.g., col. 25, lines 63-65:

Ointments are water-in-oil emulsions that contain up to 70%, but preferably from approximately 20% to approximately 50%, of water or aqueous phase. As fatty phase there come into consideration especially hydrocarbons, for example petroleum jelly, paraffin oil and/or hard paraffins, which, in order to improve the water-binding capacity, preferably contain suitable hydroxy compounds, such as fatty alcohols or esters thereof, for example cetyl alcohol or wool wax alcohols, or wool wax. Emulsifiers are corresponding lipophilic substances, such as sorbitan fatty acid esters (Spans), for example sorbitan oleate and/or sorbitan isostearate. Additives to the aqueous phase are, inter alia, humectants, such as polyalcohols, for example glycerine, propylene glycol, sorbitol and/or polyethylene glycol, and also preservatives, perfumes etc.

Accordingly, it would have been obvious to one having ordinary skill in the art to substitute the polyethylene glycol in the composition of Augurt with another glycol as the homologous propylene glycol, as taught by any one of the secondary references e.g., Herget or Baschang. One having ordinary skill in the art would reasonably expect to successfully obtain the same stable compositions due to the known functional equivalence of these glycols as taught by anyone of the numerous prior art cited by applicants. When the teaching of each reference(individually or in combination) is taken together with

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US'482, it would have been readily apparent to the one of ordinary skill in the art to envision the term substitution where the adjuvants can be substituted with the term, humectant where polyethylene or propylene glycol is effectively preventing the lactam formation via suppressing catalysis as suggested by US'482 at column 4 and claim 3(c). One would have motivated to do so, with reasonable expectation of success, because the humectants(i.e, polyethylene or propylene glycol) can effectively absorb the excessive water that is required for the lactam formation so that the water would not be available for lactam formation. One would have been motivated to modify the reference and have expected reasonable success, because they are drawn to same technical fields (constituted with same ingredients(e.g., polyethylene or propylene glycol) and share common utilities(i.e., activity of the humectant to suppress lactam formation), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Response to Arguments

Applicants submit U.S. patent no. 6,054,482 does not mention propylene glycol but discussed stability and concluded that the cause of the lactam formation was apparently also the catalytic effects of adjuvant materials which also did not follow any recognizable logic. In order to establish which

adjuvant materials promote the lactam formation, laborious serial investigations had, therefore, to be carried out. Column 4, lines 58 to 64 U.S. patent no. 6,054,482 then went on to discuss two experiments with PEG that produced opposite results when it stated in the case of the use of polyethylene glycol (PEG), cyclization to the lactam took place to a considerable extent. In another test series with very pure active substance, PEG was found to be indeed usable as an excipient. Column 5, lines 1 to 4. Accordingly, U.S. patent no. 6,054,482 demonstrated that that the stabilizing effects of PEG were at best ambiguous and that the destabilizing "catalytic effects of adjuvant materials..., did not follow any recognizable logic" so that "laborious serial investigations had, therefore, to be carried out." U.S. patent no. 6,054,482 therefore states to those skilled in the art that there is no predictability in using adjuvants to stabilize formulations, and that there is no logic that can be used to extrapolate results to other materials. Moreover, column 5, lines 11-17 and claims 4 and 8 of U.S. patent no. 6,054,482 provide a list of suitable excipients. However, this list does not include PEG. Accordingly, U.S. patent no. 6,054,482 provides no motivation for one skilled in the art to focus on PEG and no predictability of success or failure even when using PEG. Regarding U.S. patent no.

5,302,373, that patent stated that "[s]uitable humectant compounds include propylene glycol" but makes no mention of PEG.

Column 2, lines 29 to 33. Accordingly it cannot teach that propylene glycol is a functional equivalent of PEG. Moving to

U.S. patent no. 5,618,342, that patent disclosed PEG and polypropylene glycol as humectants. Column 2, lines 37 to 41. However, one skilled in the art recognizes that polypropylene glycol is not the same as propylene glycol, and therefore that

U.S. patent no. 5,618,342 does not teach that PEG and polypropylene glycol are functional equivalents. Finally, U.S. patent no. 4,666,886, discloses that PEG and propylene glycol are humectants, but only in the context of ointments and creams. Nothing motivates the reader to combine the teachings of U.S. patent no. 4,666,886 with those of U.S. patent no. 6,054,482 which, as already noted, teaches that the art is unpredictable.

In reply, One cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968). The test for obviousness under 35 USC 103 is not the express suggestion of the claimed invention in any or all of the references but what the references taken collectively would suggest; and inferences which one skilled in the art would reasonably be expected to draw from the disclosure in the

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references. In re Preda, 159 USPQ 342 and In re Conrad, 169 UASPQ 170. The suggested teachings of Augart et al (US 6,054,482) ('482 patent) as to the lactam formation, albeit a laborious one, suffices the finding of obviousness. Obviousness does not require absolute predictability. Thus, the combined teachings of the prior art would lead one to the claimed composition.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571 272-0763. The fax phone number for the

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organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/T. D. Wessendorf/

Primary Examiner, Art Unit 1639

May 26, 2008

<i>Application Number</i> 	Application/Control No.	Applicant(s)/Patent under Reexamination	
	09/674,819	AOMATSU, AKIRA	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	